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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR		ATTORNEY DOCKET NO.
09/258,217	02/26/99	KEATING	M	2323-127

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EXAMINER	
CHEN, S	
ART UNIT	**PAPER NUMBER**
1633	11

DATE MAILED: 07/25/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/258,217	Applicant(s) Keating et al.
	Examiner Shin-Lin Chen	Group Art Unit 1633

☒ Responsive to communication(s) filed on *May 11, 2000*

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

☒ Claim(s) *1-6, 9, and 10* is/are pending in the applicat

Of the above, claim(s) _____ is/are withdrawn from consideration

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-6, 9, and 10* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

— SEE OFFICE ACTION ON THE FOLLOWING PAGES —

DETAILED ACTION

the amendment filed 5-11-00 (Paper No. 9) and declaration (Paper No. 10) have been entered. Claims 1, 3, 5, 6 and 9 have been amended. Claims 7, 8 and 11-14 have been canceled. Claims 1-6, 9 and 10 are pending.

Claim Rejections - 35 USC § 102

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

2. Claims 2 and 4 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Sechler et al., 1994 (U).

Claim 2 is directed to a mouse comprising a genome with no functional elastin gene. Claim 4 is directed to a mouse cell comprising a genome with no functional elastin gene.

Sechler discloses construction of transgenic mice that contain rat tropoelastin gene (elastin gene) lacking exon sequences within the 5' or 3' end of the gene, e.g. lacking exon 33 or exons 19-31. The transgenic mice disclosed by Sechler includes hemizygous ELN +/- and homozygous ELN -/-, wherein the homozygous ELN-/- does not have functional elastin gene in the genome. The mice set forth above contain mouse cells comprising a genome with no functional elastin gene. Thus the claims are clearly anticipated by Sechler.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. Claims 1-4 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sechler et al., 1995 (U) in view of Wydner et al., 1994 (X2).

Claims 1 and 3 are directed to a mouse or a mouse cell comprising one functional mouse elastin gene and either one nonfunctional or no second mouse elastin gene in its genome. Claims 2 and 4 are directed to a mouse or a mouse cell comprising a genome with no functional elastin gene.

Sechler teaches construction of transgenic mice that contain rat tropoelastin gene (elastin gene) lacking exon sequences within the 5' or 3' end of the gene, e.g. lacking exon 33 or exons 19-31 (e.g. p. 151, 152). The transgenic mice disclosed by Sechler et al. includes hemizygous ELN +/- and homozygous ELN -/-. The mice set forth above contain mouse cells comprising a genome with no functional elastin gene. Sechler also teaches that there are a variety of disorders characterized by abnormal elastin synthesis and a concomitant deposition of aberrant elastic fiber, such as hypertension, atherosclerosis, actinic elastosis, Marfan's syndrome and SVAS, and mutations in the tropoelastin gene (elastin gene) plays a role in analogous human disorders of

elastic tissue, including SVAS (e.g. p. 149). Sechler teaches using the transgenic mice having mutated elastin gene to study the role of elastin gene in analogous human disorder such as SVAS.

Sechler does not teach the availability of mouse elastin gene for making a mouse containing mutated mouse elastin gene.

Wydner teaches the complete cDNA sequence of mouse tropoelastin (elastin) gene and the mutations in the tropoelastin gene are strongly implicated in supravalvular aortic stenosis (SVAS), a heritable vascular disorder that maps to chromosome 7 (e.g. introduction, p. 128, 129).

It would have been obvious for one of ordinary skill in the art at the time of the invention to substitute the rat elastin gene with a mouse elastin gene as taught by Wydner to make homozygous or heterozygous transgenic mice or mouse cells having mutated mouse elastin gene as taught by Sechler.

One having ordinary skill at the time the invention was made would have been motivated to produce heterozygous or homozygous transgenic mice or mouse cells having mutated mouse elastin gene in order to study the role of elastin gene in analogous human disorder such as SVAS because Sechler teaches that there are a variety of disorders characterized by abnormal elastin synthesis and a concomitant deposition of aberrant elastic fiber, such as hypertension, atherosclerosis, actinic elastosis, Marfan's syndrome and SVAS.

5. Claims 5, 6, 9 and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Reitamo et al., 1994 (V) in view of Sechler et al., 1995 (U) and Wydner et al., 1994 (X2).

Claim 5 is directed to a method to screen for drug candidates useful for treating humans with SVAS, hypertension or atherosclerosis by using an ELN +/- mouse or human, wherein said drug candidates inhibit occlusion of arteries. Claim 6 is directed to a method to screen for drug candidates useful for treating humans with atherosclerosis, SVAS or essential hypertension by measuring activity of elastase in the presence of drugs wherein said drugs which inhibit elastase are said drug candidates. Claims 9 and 10 are directed to a method to screen for drug candidates useful for treating humans with SVAS, hypertension or atherosclerosis by using ELN +/- mouse or human, or ELN +/- mouse or human cells and by measuring the synthesis of elastin RNA and elastin, respectively.

Reitamo teaches generating transgenic mice expressing a human elastin promoter/CAT reporter gene construct and injecting IL-10 subcutaneously into said transgenic mice. Reitamo et al. also teach a method of screening a compound which can stimulate the elastin promoter *in vivo or in vitro,* and show IL-10 up-regulates elastin gene expression *in vivo* by CAT assay (transgenic mice skin) and *in vitro* by measuring the elastin mRNA level using Northern analysis (e.g. abstract, p. 332).

Reitamo does not teach using ELN +/- mice or ELN +/- cells to screen drug candidate useful for treating atherosclerosis hypertension or SVAS in a human by measuring the synthesis of elastin or screen drug which inhibits occlusion of arteries.

Sechler teaches construction of transgenic mice that contain rat tropoelastin gene (elastin gene) lacking exon sequences within the 5' or 3' end of the gene, e.g. lacking exon 33 or exons 19-31 (e.g. p. 151, 152). The transgenic mice disclosed by Sechler includes hemizygous ELN +/- and homozygous ELN -/-. The mice set forth above contain mouse cells comprising a genome with no functional elastin gene. Sechler also teaches that there are a variety of disorders characterized by abnormal elastin synthesis and a concomitant deposition of aberrant elastic fiber, such as hypertension, atherosclerosis, actinic elastosis, Marfan's syndrome and SVAS, and mutations in the tropoelastin gene (elastin gene) plays a role in analogous human disorders of elastic tissue, including SVAS (e.g. p. 149). Sechler teaches using the transgenic mice having mutated elastin gene to study the role of elastin gene in analogous human disorder such as SVAS.

Wydner teaches the complete cDNA sequence of mouse tropoelastin (elastin) gene and the mutations in the tropoelastin gene are strongly implicated in supravalvular aortic stenosis (SVAS), a heritable vascular disorder that maps to human chromosome 7 (e.g. introduction, p. 128, 129).

It would have been obvious for one of ordinary skill in the art at the time of the invention to substitute the rat elastin gene with a mouse elastin gene as taught by Wydner to make homozygous or heterozygous transgenic mice or mouse cells having mutated mouse elastin gene as taught by Sechler. The mutation of elastin gene is associated with SVAS, an inherited obstructive vascular disease that affects the aorta, carotid, coronary and pulmonary arteries. It would have been obvious for one of ordinary skill to use the ELN +/- mice or ELN +/- mouse

cells as taught by Wydner and Sechler to screen for drugs or compounds useful for treating humans with SVAS, hypertension or atherosclerosis which are diseases associated with arteries.

One having ordinary skill at the time the invention was made would have been motivated to produce heterozygous or homozygous transgenic mice or mouse cells having mutated mouse elastin gene in order to study the role of elastin gene in analogous human disorder such as SVAS. One having ordinary skill at the time the invention was made would have been motivated to use the ELN +/- mice or mouse cells as taught by Wydner and Sechler to screen for drugs or compounds useful for treating SVAS, atherosclerosis or hypertension in a human by measuring the synthesis of elastin mRNA or elastin, or the drug or compound which can inhibit the occlusion of arteries because the implication of the correlation of SVAS, hypertension and atherosclerosis with the elastin gene as taught by Sechler and Wydner, and the discovery of such compounds would have been useful for treating humans with SVAS, hypertension or atherosclerosis.

Conclusion

No claims is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shin-Lin Chen whose telephone number is (703) 305-1678. The examiner can normally be reached on Monday to Friday from 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader can be reached on (703) 308-0447. The fax phone number for this group is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist, whose telephone number is (703) 308-0196.

Deborah Clark

DEBORAH J.R. CLARK
PRIMARY EXAMINER

Shin-Lin Chen, Ph.D.